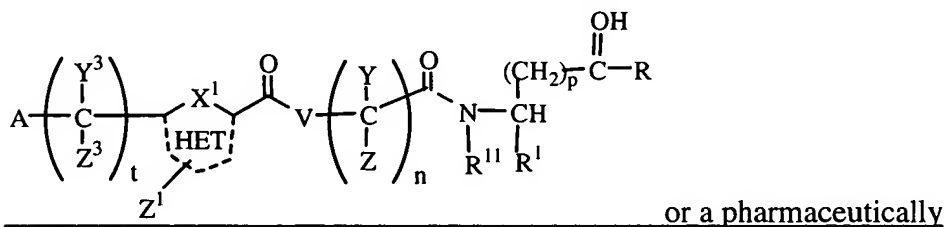


III. Amendments to the Claims

Cancel claims 1-12. Please amend claims 13-22 as follows:

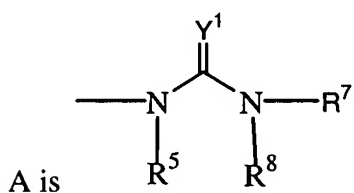
Claims 1-12 (Cancelled)

Claim 13 (Currently Amended) A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering a therapeutically effective $\alpha_v\beta_3$ inhibiting amount of a compound according to Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 of Formula I:



acceptable salt thereof, wherein

HET is a 5-8 membered monocyclic heterocyclic ring, optionally unsaturated, containing 1 to 4 heteroatoms, selected from the group consisting of O, N, or S, wherein X¹ is selected from the group consisting of CH, CH₂, N, NH, O and S;



wherein Y¹ is selected from the group consisting of N—R², O, and S;

R² is selected from the group consisting of H; alkyl; aryl; hydroxy; alkoxy; cyano; nitro; amino; alkenyl; alkynyl; amido; alkylcarbonyl; arylcarbonyl; alkoxy carbonyl; aryloxy carbonyl; haloalkylcarbonyl; haloalkoxy carbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxy carbonyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen,

hydroxyl, haloalkyl, cyano, nitro, carboxyl, amino, alkoxy, aryl or aryl optionally substituted with one or more halogen, haloalkyl, lower alkyl, alkoxy, cyano, alkylsulfonyl, alkylthio, nitro, carboxyl, amino, hydroxyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, hydroxy, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, cyano, nitro, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, carboxyl derivatives, amino, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycle; monocyclic heterocycles; and monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, aryl or fused aryl; or

R² taken together with R⁷ forms a 4-12 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, thioalkyl, alkylamino, hydroxy, keto, alkoxy, halo, phenyl, amino, carboxyl or carboxyl ester, spirodioxolane, and fused phenyl;
or

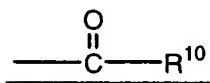
R² taken together with R⁷ forms a 4-12 membered heterocycle, optionally unsaturated, containing one or more heteroatom selected from O, N and S; or

R² taken together with R⁷ forms a 5-9 membered heteroaromatic ring optionally substituted with one or more substituent selected from lower alkyl, phenyl, alkoxy and hydroxy;

R² taken together with R⁷ forms a 5 membered heteroaromatic ring fused with a aryl or heteroaryl ring;

R⁷ (when not taken together with R²) and R⁸ are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; aralkyl; amino; alkylamino; hydroxy; alkoxy; arylamino; amido; alkylcarbonyl; arylcarbonyl; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; cycloalkyl; bicycloalkyl; aryl; acyl; benzoyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen, hydroxy, haloalkyl, cyano, nitro, carboxyl derivatives, amino, alkoxy, thio, alkylthio, sulfonyl, aryl, aralkyl, aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethyl, sulfonyl, alkylsulfonyl, haloalkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles or fused monocyclic heterocycles; [monocyclic heterocycles;] monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, aryloxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, aryl, fused aryl; monocyclic and

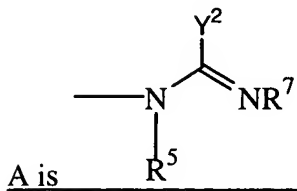
bicyclic heterocyclicalkyls; $-\text{SO}_2\text{R}^{10}$ — wherein R^{10} is selected from the group consisting of alkyl, aryl and monocyclic heterocycles, all optionally substituted with one or more substituent selected from the group consisting of halogen, haloalkyl, alkyl, alkoxy, cyano, nitro, amino, acylamino, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, trifluoromethylthio, trifluoroalkoxy, trifluoromethylsulfonyl, aryl, aryloxy, thio, alkylthio, and monocyclic heterocycles; and



wherein R^{10} is defined above; or

NR^7 and R^8 taken together form a 4-12 membered mononitrogen containing monocyclic or bicyclic ring optionally substituted with one or more substituent selected from lower alkyl, carboxyl derivatives, aryl or hydroxy and wherein said ring optionally contains a heteroatom selected from the group consisting of O, N, and S;

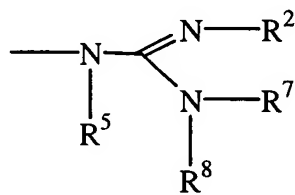
R^5 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, benzyl, and phenethyl; or



wherein Y^2 is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles; alkyl optionally substituted with aryl which can also be optionally substituted with one or more substituent selected from halo, haloalkyl, alkyl, nitro, hydroxy, alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkynyl; alkenyl; $-S-R^9$ and $-O-R^9-$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen and monosulfur or monooxygen containing heterocyclic ring optionally substituted with lower alkyl, hydroxy, keto, phenyl, carboxyl or carboxyl ester, and fused phenyl or R^9 taken together with R^7 as thiazole, oxazole, benzoxazole, or benzothiazole; and

R^5 and R^7 are as defined above; or

Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen or dinitrogen containing ring optionally substituted with alkyl, aryl, keto or hydroxy; or



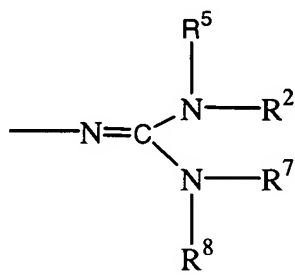
A is _____

Where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the

group consisting of lower alkyl, hydroxy, alkoxy, keto, phenyl, or carboxy derivatives; and R⁸ is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxy carbonyl, aryloxy carbonyl, haloalkylcarbonyl, haloalkoxy carbonyl, alkylthiocarbonyl, arylthiocarbonyl, or acyloxymethoxy carbonyl; and

R⁵ is defined as above; or

R² and R⁷ taken together form a imidazole or pyrimidone; or



A is

where R² and R⁷ taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with hydroxy, keto, phenyl, or alkyl; and

R⁸ and R⁵ are both selected for the group consisting of alkylcarbonyl, arylcarbonyl, alkoxy carbonyl, aryloxy carbonyl, haloalkylcarbonyl, haloalkoxy carbonyl, alkylthiocarbonyl, arylthiocarbonyl and acyloxymethoxy carbonyl;

Z¹ is one or more substituent selected from the group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; halogen; haloalkyl; haloalkoxy; nitro; amino; aminoalkyl; alkylamino; acylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; triacetamide; acetamide; acyl; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

V is selected from the group consisting of –N-(R⁶)- wherein R⁶ is selected from the group consisting of H; lower alkyl; cycloalkyl; aralkyl; aryl; and monocyclic heterocycles; or R⁶ taken together with Y, forms a 4-12 membered mononitrogen containing ring;

Y, Y³, Z and Z³ are independently selected from the group consisting of hydrogen; alkyl; aryl; and cycloalkyl; or Y and Z taken together form a cycloalkyl; or Y³ and Z³ taken together form a cycloalkyl;

N is an integer 1, 2, or 3;

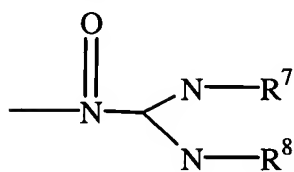
t is an integer 0, 1, or 2;

p is an integer 0, 1, 2, or 3;

R is X—R³ wherein X is selected from the group consisting of O, S and NR⁴, wherein R³ and R⁴ are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; haloalkyl; aryl; arylalkyl; sugars; steroids; polyalkylethers; alkylamido; alkyl N,N-dialkylamido; pivaloyloxymethyl; and in the case of the free acid, all pharmaceutically acceptable salts thereof;

R¹ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, carboxyl derivatives; haloalkyl; cycloalkyl; monocyclic heterocycles; monocyclic heterocycles optionally substituted with one or more substituent selected from the group consisting of alkyl, halogen, haloalkyl, cyano, hydroxy, aryl, fused aryl, nitro, alkoxy, aryloxy, alkylsulfonyl, arylsulfonyl, sulfonamide, thio, alkylthio, carboxyl derivatives, amino, amido; alkyl optionally substituted with one or more of halo, haloalkyl, hydroxy, alkoxy, aryloxy, thio, alkylthio, alkynyl, alkenyl, alkyl, arylthio, alkylsulfoxide, alkylsulfonyl, arylsulfoxide, arylsulfonyl, cyano, nitro, amino, alkylamino, dialkylamino, alkylsulfonamide, arylsulfonamide, acylamide, carboxyl derivatives, sulfonamide, sulfonic acid, phosphonic acid

derivatives, phosphinic acid derivatives, aryl, arylthio, arylsulfoxide, or arylsulfone all optionally substituted on the aryl ring with halo, alkyl, haloalkyl, cyano, nitro, hydroxy, carboxyl derivatives, alkoxy, aryloxy, amion, alkylamino, dialkylamino, amido, aryl, fused aryl, monocyclic heterocycles; and fused monocyclic heterocycles, monocyclic heterocyclicthio, monocyclic heterocyclicsulfoxide, and monocyclic heterocyclic sulfone, which can be optionally substituted with halo, haloalkyl, nitro, hydroxy, alkoxy fused aryl, or alkyl;alkylcarbonyl, haloalkylcarbonyl, and arylcarbonyl; aryl optionally substituted in one or more positions with halo, haloalkyl, alkyl, alkoxy, aryloxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, acyloxy, carboxyl derivatives, carboxyalkoxy; amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles and fused heterocycles; and



wherein R⁷ and R⁸ are defined as above and provided that taken together with the nitrogen, R⁷ and R⁸ comprise an amino acid; and R¹¹ is selected from the group consisting of H, alkyl, aralkyl, alkenyl, alkylnyl, haloalkyl or haloalkylnyl or R¹¹ taken together with Y forms a 4-12 membered mononitrogen containing ring.

Claim 14 (Original) A method according to Claim 13 wherein the condition treated is tumor metastasis.

Claim 15 (Original) A method according to Claim 13 wherein the condition treated is solid tumor growth.

Claim 16 (Original) A method according to Claim 13 wherein the condition treated is angiogenesis.

Claim 17 (Original) A method according to Claim 13 wherein the condition treated is osteoporosis.

Claim 18 (Original) A method according to Claim 13 wherein the condition treated is humoral hypercalcemia of malignancy.

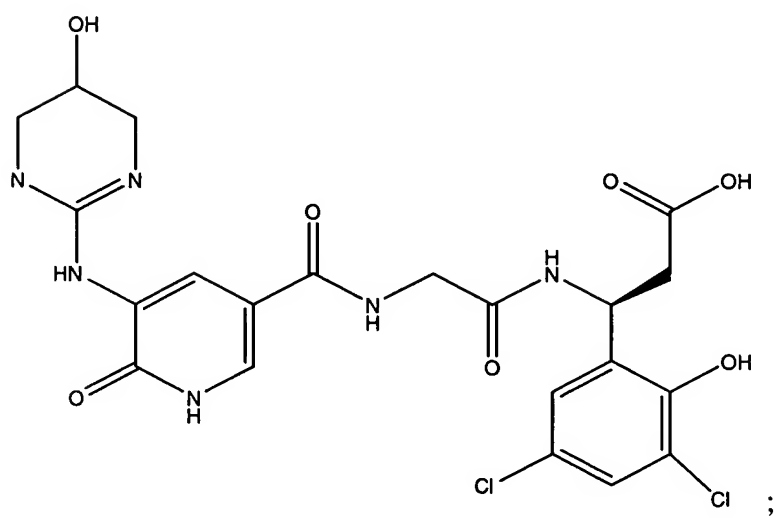
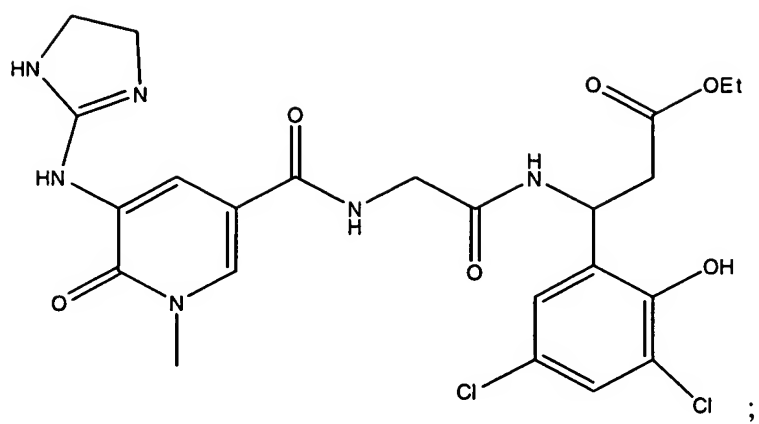
Claim 19 (Original) A method according to Claim 13 wherein the condition treated is smooth muscle cell migration.

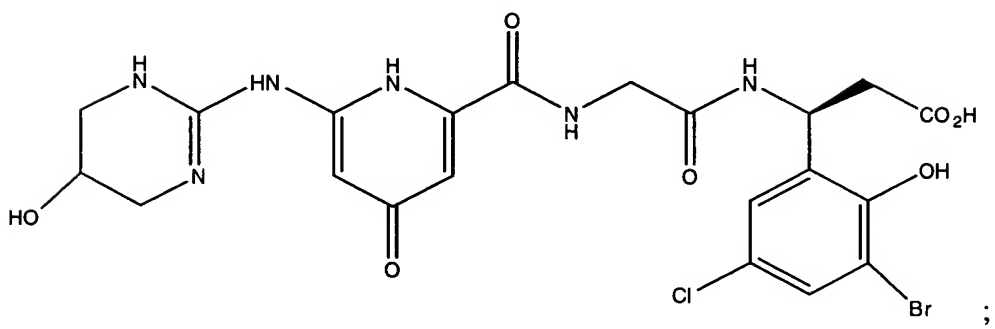
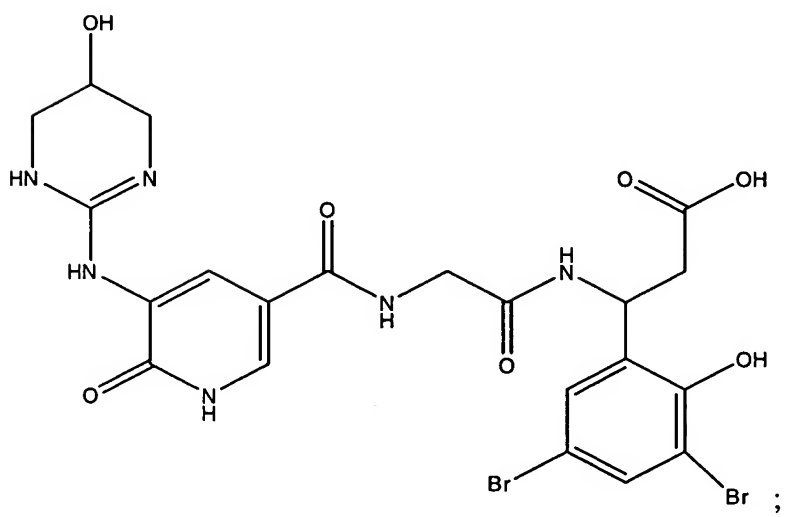
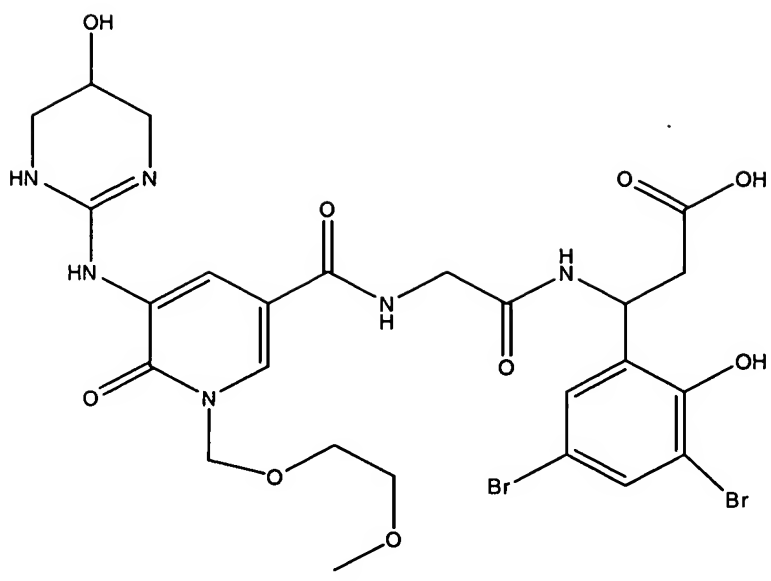
Claim 20 (Original) A method according to Claim 13 wherein restenosis is inhibited.

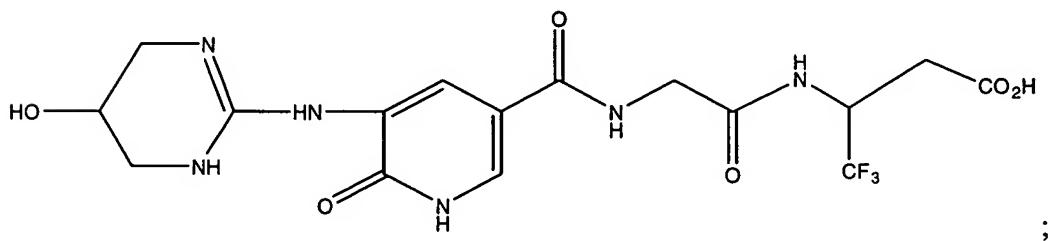
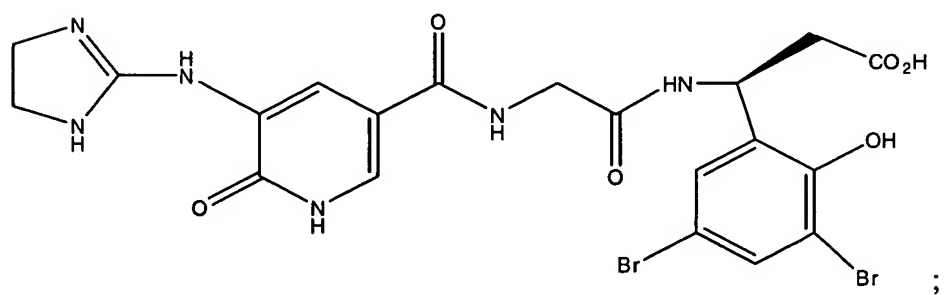
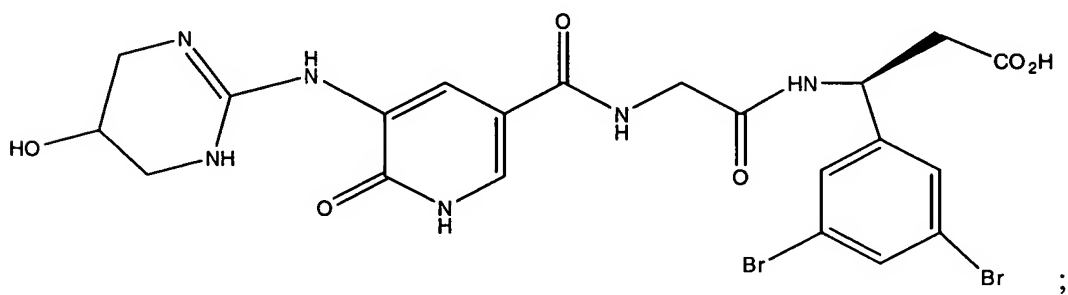
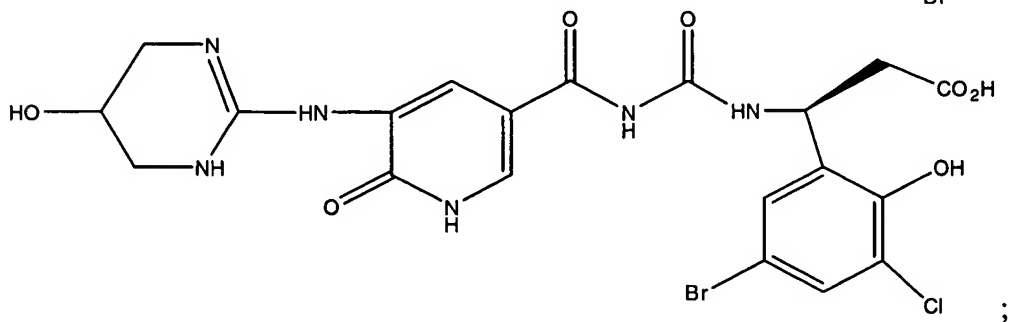
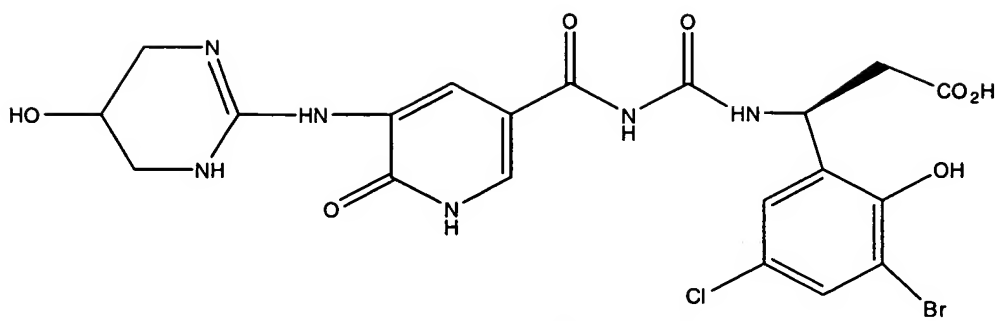
Claim 21 (Original) A method according to Claim 13 wherein the condition treated is rheumatoid arthritis.

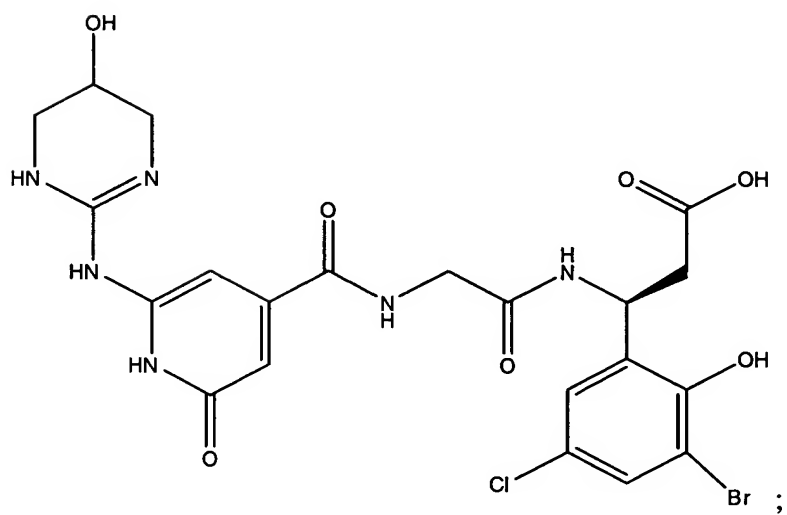
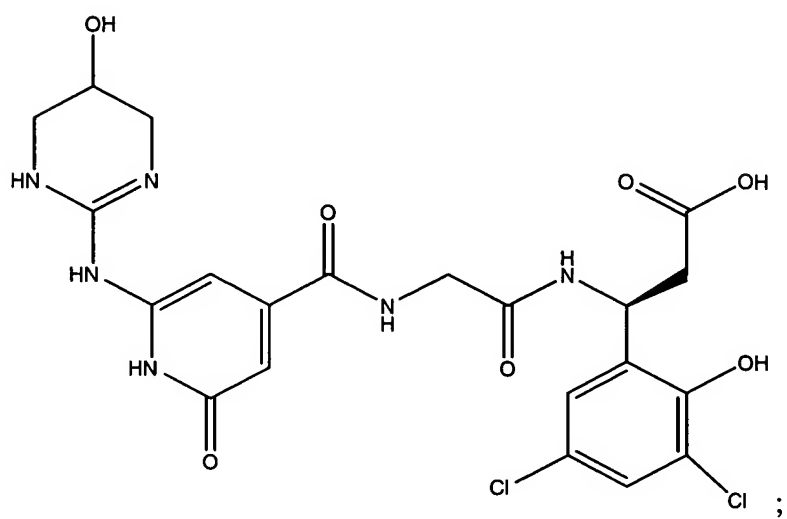
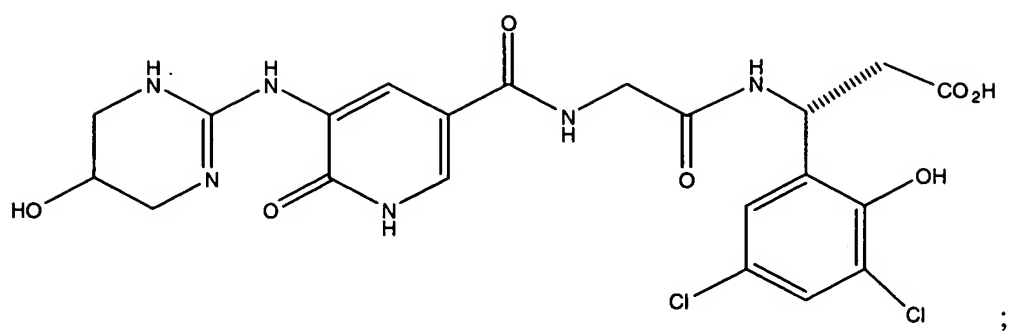
Claim 22 (Original) A method according to Claim 13 wherein the condition treated is macular degeneration.

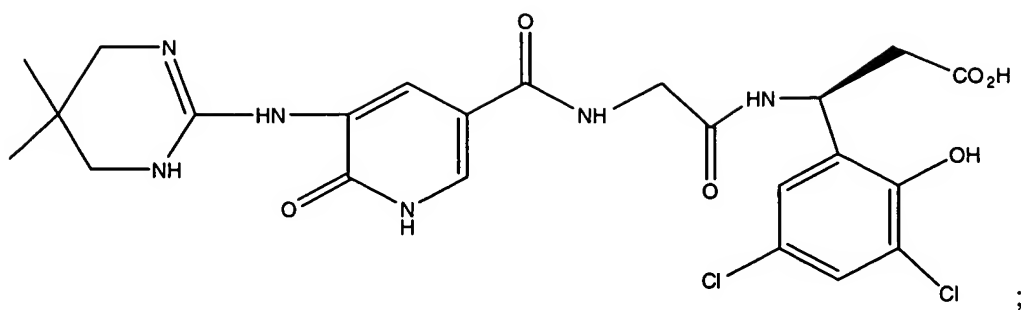
Claim 23 (New) A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering a therapeutically effective $\alpha_v\beta_3$ inhibiting amount of a compound selected from the group consisting of



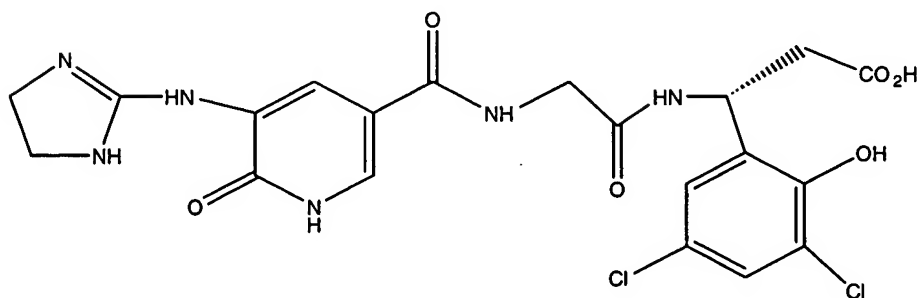








and



Claim 24 (New) The method of Claim 23 wherein the condition treated is selected from the group consisting of tumor metastasis, solid tumor growth, angiogenesis, osteoporosis, humoral hypercalcemia of malignancy, smooth muscle cell migration, restenosis, rheumatoid arthritis, and macular degeneration.